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What is claimed is:

5 1. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising generating a library of nucleobase sequences *in silico* according to defined criteria.

10 2. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria.

15 3. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising robotically synthesizing a plurality of defined oligonucleotide compounds.

20 4. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

25 5. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising generating a library of nucleobase sequences *in silico* according to defined criteria and evaluating *in silico* a plurality of virtual oligonucleotides having said
30 nucleobase sequences according to defined criteria.

35 6. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria and robotically synthesizing a plurality of oligonucleotide

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compounds corresponding to said plurality of virtual oligonucleodites.

5 7. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria and robotically assaying a plurality of oligonucleotide compounds corresponding to said virtual oligonucleotides
10 for one or more desired physical, chemical or biological properties.

15 8. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising generating a library of nucleobase sequences *in silico* according to defined criteria and robotically synthesizing a plurality of oligonucleotide compounds having said nucleobase sequences.

20 9. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising robotically synthesizing a plurality of oligonucleotide compounds and robotically assaying said plurality of oligonucleotide compounds for one or more
25 desired physical, chemical or biological properties.

30 10. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising generating a library of nucleobase sequences *in silico* according to defined criteria and robotically assaying a plurality of oligonucleotide compounds having said nucleobase sequences for one or more desired physical, chemical or biological properties.

35 11. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence,

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comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

5 (b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria; and

(c) robotically synthesizing a plurality of oligonucleotide compounds.

10 12. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

15 (b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria; and

20 (c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

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13. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

25 (a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) robotically synthesizing a plurality of oligonucleotide compounds; and

30 (c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

14. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

35 (a) evaluating *in silico* a plurality of virtual

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oligonucleotides according to defined criteria;

(b) robotically synthesizing a plurality of oligonucleotide compounds; and

(c) robotically assaying a plurality of
5 oligonucleotide compounds for one or more desired physical, chemical or biological properties.

15. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence,
10 comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a)
15 according to defined criteria;

(c) robotically synthesizing a plurality of oligonucleotide compounds; and

(d) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.
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16. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

25 (a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) choosing an oligonucleotide chemistry;

(c) robotically synthesizing a set of oligonucleotide compounds having said nucleobase sequences of step (a) and said oligonucleotide chemistry of step (b);
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(d) robotically assaying said set of oligonucleotide compounds of step (c) for a physical, chemical or biological activity; and

(e) selecting a subset of said set of oligonucleotide compounds of step (c) having a desired level of physical, chemical or biological activity in order to generate said
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set of compounds.

17. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) choosing an oligonucleotide chemistry;

(c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) and the oligonucleotide chemistry of (b) according to defined criteria, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

(d) robotically synthesizing a set of oligonucleotide compounds having said preferred nucleobase sequences of step (c) and said oligonucleotide chemistry of step (b);

(e) robotically assaying said set of oligonucleotide compounds of step (d) for a physical, chemical or biological activity; and

(f) selecting a subset of said set of oligonucleotide compounds of step (d) having a desired level of physical, chemical or biological activity in order to generate said set of compounds.

18. The method of claim 4, wherein said step of robotically assaying said plurality of oligonucleotide compounds is performed by computer-controlled real-time polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

19. The method of claim 1, wherein said target nucleic acid sequence is that of a genomic DNA, a cDNA, a product of a polymerase chain reaction, an expressed sequence tag, an mRNA or a structural RNA.

20. The method of claim 1, wherein said target nucleic acid sequence is a human nucleic acid.

5 21. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising generating a library of antisense nucleobase sequences *in silico* according to defined criteria.

10 22. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria.

15 23. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising robotically synthesizing a plurality of antisense compounds.

9 20 24. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising robotically assaying a plurality of antisense compounds for one or more desired physical, chemical or biological properties.

25 25. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising generating a library of nucleobase sequences *in silico* according to defined criteria and evaluating *in silico* a plurality of virtual oligonucleotides having said
30 nucleobase sequences according to defined criteria.

35 26. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria and robotically synthesizing a plurality of oligonucleotide

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compounds.

27. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria and robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

28. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising generating a library of nucleobase sequences *in silico* according to defined criteria and robotically synthesizing a plurality of oligonucleotide compounds having said nucleobase sequences.

29. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising robotically synthesizing a plurality of oligonucleotide compounds and robotically assaying said plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

30. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising generating a library of nucleobase sequences *in silico* according to defined criteria and robotically assaying a plurality of oligonucleotide compounds having said nucleobase sequences for one or more desired physical, chemical or biological properties.

31. A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising the steps of:

(a) generating a library of nucleobase sequences in

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silico according to defined criteria;

(b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria; and

5 (c) robotically synthesizing a plurality of oligonucleotide compounds.

32. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the
10 steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria; and
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(c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

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20 33. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

25 (b) robotically synthesizing a plurality of oligonucleotide compounds; and

(c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

30 34. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

(a) evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria;
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(b) robotically synthesizing a plurality of

oligonucleotide compounds; and

(c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

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35. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

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(b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria;

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(c) robotically synthesizing a plurality of oligonucleotide compounds; and

(d) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

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36. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

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(b) choosing an oligonucleotide chemistry;

(c) robotically synthesizing a set of oligonucleotide compounds having said nucleobase sequences of step (a) and said oligonucleotide chemistry of step (b);

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(d) robotically assaying said set of oligonucleotide compounds of step (c) for a physical, chemical or biological activity; and

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(e) selecting a subset of said set of oligonucleotide compounds of step (c) having a desired level of physical, chemical or biological activity in order to generate said set of compounds.

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37. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

- 5 (a) generating a library of nucleobase sequences *in silico* according to defined criteria;
- (b) choosing an oligonucleotide chemistry;
- 10 (c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;
- (d) robotically synthesizing a set of oligonucleotide compounds having said preferred nucleobase sequences of step (b) and said oligonucleotide chemistry of step (c);
- 15 (e) robotically assaying said set of oligonucleotide compounds of step (d) for a physical, chemical or biological activity; and
- 92 (f) selecting a subset of said set of oligonucleotide compounds of step (d) having a desired level of physical, chemical or biological activity in order to generate said set of compounds.
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38. The method of claim 24, wherein said step of robotically assaying said plurality of nucleic acid sequences is performed by computer-controlled real-time polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

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39. The method of claim 21, wherein said nucleic acid sequence is that of a genomic DNA, a cDNA, a product of a polymerase chain reaction, an expressed sequence tag, an mRNA or a structural RNA.

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40. The method of claim 21, wherein said nucleic acid sequence is a human nucleic acid.

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41. A computer formatted medium comprising computer readable instructions for identifying active compounds.

42. A computer formatted medium comprising computer readable instructions for performing the method of any one of claims 1 to 20.

43. A computer formatted medium comprising computer readable instructions for performing a method of identifying one or more nucleic acid sequences amenable to antisense modulation.

44. A computer formatted medium comprising computer readable instructions for performing the method of any one of claims 21 to 40.

45. A computer formatted medium comprising one or more nucleic acid sequences amenable to antisense modulation in computer readable form.

46. A computer formatted medium comprising one or more nucleic acid sequences amenable to antisense modulation in computer readable form, wherein said one or more nucleic acid sequences is identified according to the method of any one of claims 21, 22 or 24-40.

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